Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA

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This document supersedes 510(k) Sterility Review Guidance K90-1, dated February 12, 1990.

U.S. Department Of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Office of Device Evaluation

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance contact Timothy A. Ulatowski at (301) 443-8879 or by email tau@cdrh.fda.gov.

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This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the Food and Drug Administration (FDA) or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

Background

This guidance serves to update the Office of Device Evaluation's (ODE'S) review procedures regarding sterilization data submitted in premarket notification (510(k)) submissions as outlined in Blue Book Memorandum #K90-1 issued on February 12, 1990. Since our issuance of the original memorandum, there have been significant changes in the regulatory environment that has made aspects of the original memorandum obsolete. Specifically,

1. promulgation of the Quality System regulation (QS regulation, 21 CFR 820) in 1996;

2. issuance of Blue Book Memorandum #K97-1 regarding changes to devices that can be made without submitting 510(k)s; and

3. enactment of the Food and Drug Administration (FDA) Modernization Act of 1997 (FDAMA), which among many things, separated compliance with QS requirements from substantial equivalence in most cases.

In 1997, the Center for Devices and Radiological Health (CDRH) decided that the effectiveness of a device manufacturer's sterilization processes would best be ensured through compliance with the QS regulation rather than through 510(k) review. This decision was communicated to ODE staff and the medical device industry in Blue Book Memorandum #K97-1, where CDRH stated that changes in sterilization processes do not require 510(k) clearance, unless the changes significantly alter the properties/specifications of a device or result in a lower sterility assurance level (SAL). In instances where a manufacturer concludes that a change in sterilization method has not significantly affected device properties/specifications or resulted in a lower SAL, no 510(k) need be submitted, but rather the appropriate documentation must be maintained at the manufacturing site in accordance with the QS regulation requirements.

The enactment of FDAMA emphasized the separation between issues of compliance with the QS regulation and determinations of substantial equivalence (SE) with a new

provision that instructs the agency not to withhold SE determinations for noncompliance with any statutory provisions unrelated to the classification decision unless there is a substantial likelihood that the failure to comply will potentially present a serious risk to health. This new provision, Section 513(f)(5) of the Federal Food, Drug, and Cosmetic Act, specifically includes noncompliance with good manufacturing practices (now referred to as QS requirements) as a failure that should not ordinarily delay an SE decision. These events have prompted us to revise our procedures for the review of sterilization information in all 510(k) submissions.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

Methods of Sterilization

There are two types of sterilization methods used to sterilize medical devices - traditional and non-traditional. The specific methods for each type are below.

Traditional Methods of Sterilization

Traditional methods of sterilization include:

- Dry heat sterilization, as described in CDRH-recognized standards
- EtO with devices placed in a fixed chamber
- Steam
- Radiation (gamma and electron beam)

Non-Traditional Methods of Sterilization

In general, methods of sterilization outside the scope of specific CDRH-recognized standards are non-traditional. As of the date of this memorandum, non-traditional methods of sterilization include:

- EtO in which EtO is injected into a porous polymer bag. Terms used for this process include:

    - "bag method"
    - "diffusion method"
    - "sterilization pouch"
    - "injection method"
    - "validation parts 'A' and 'B'"

  Less common indicators are
    - a long gas dwell time (>8 hours) or the absence of a specified gas dwell time
    - use of EtO volume (e.g., 7.2 gr) instead of concentration (e.g., 500 - 600 mg/l)
    - mention of EtO (or gas) cartridge
    - use of humidichips
    - use of "100% EtO in-house"

- High intensity light
- Chlorine dioxide
- Ultraviolet light
- Gas plasma
- Vapor systems (e.g., peroxide or peracetic acid)
- Filtration methods
- Liquid chemical sterilization or high level disinfection as the terminal process, except:
    - Limited use of a liquid peracetic acid system in endoscopy and with metal instruments
    - Limited use of liquid germicides for some biologic origin devices

A new method remains a non-traditional method unless and until:

(1) CDRH evaluates the validation data for the method of sterilization as part of a quality system evaluation and finds it satisfactory for that general type of device; or

(2) The specific sterilization method is incorporated into a new or existing voluntary consensus standard formally recognized by the Agency.

Review Procedures for Traditional and Non-Traditional Sterilization Methods

The following procedures apply to all 510(k)s for devices labeled as sterile, regardless of the method of sterilization. ODE scientific reviewers should gather and review the following sterilization information when evaluating 510(k)s for sterile devices:

- the sterilization method that will be used (e.g., dry heat, ethylene oxide (EtO), steam, radiation);
- a description of the method that will be used to validate the sterilization cycle, but not the validation data itself;
- a description of the packaging to maintain the device's sterility, not including package integrity testing data;
- if sterilization involves EtO, the maximum levels of residues of EtO and ethylene chlorhydrin which remain on the device (note: ethylene glycol residue level was dropped from this updated guidance because the recognized standard, ISO 10993-7, does not include measurement of ethylene glycol residues);
- if the product is labeled "pyrogen free," a description of the method used to make the determination, e.g., limulus amebocyte lysate (LAL);
- the sterility assurance level specification (SAL) (e.g., 10^{-6} for all devices, except 10^{-3} for devices only contacting intact skin); and
- in the case of radiation sterilization, the radiation dose.

Additional Procedures for 510(k)s Citing Non-Traditional Sterilization Methods

A manufacturer's use of a non-traditional sterilization method should not ordinarily effect or delay a substantial equivalence determination. For each 510(k) citing a non-traditional method of sterilization, however, scientific reviewers should notify their Branch Chief and proceed as described below. In general, situations involving non-traditional sterilization methods should be brought to the Office of Compliance's (OC) attention so they can determine whether conducting an inspection of the sterilization facility is a priority.

In order to maintain consistency in our approach to non-traditional methods of sterilization, we recommend that review scientists:

1. Identify the section in the submission related to a potential non-traditional method of sterilization; and

2. refer a copy of the section to the Branch Chief, Infection Control Devices (INCB), Division of Dental, Infection Control and General Hospital Devices (DDIGD) for consideration.

INCB will assess the information and provide feedback to the referring ODE division. If INCB determines that the method is actually a traditional method, then INCB will advise the referring ODE division. If INCB determines it is a non-traditional method, INCB will advise the referring ODE division and direct the information to OC for appropriate action. INCB will provide technical consultation to OC in the follow-up period, as each situation requires.

Effective Date: These procedures are effective immediately.